PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference TP-04049-PCT	Date of mailing *(day/month/year)* **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2005/000638	20.01.2005	21.01.2004

International Patent Classification (IPC) or both national classification and IPC

Applicant

TORAY INDUSTRIES, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

The common technical matter for the inventions of claims 1, 15 and 24 as independent claims is fractionation of a protein using a membrane.

However, since the aforementioned matter is found to have been well known before the filing of this application as described in, for example, "JP, 2001-200000, A", the common matter is no more than the prior art, and cannot be said to be a special technical matter in PCT Rule 13.2. Therefore, the inventions of claims are not found to be a group of inventions so linked as to form a single general inventive concept. In consideration of independent claims and related techniques, the International Examining Authority finds that the inventions of this application can be grouped into the following three groups of inventions:

(1) claims 1-14,
(2) claims 15-23, and
(3) claims 24-27.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☒ all parts

   ☐ the parts relating to claims Nos. _____

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	3, 5, 8-27	YES
	Claims	1, 2, 4, 6, 7	NO
Inventive step (IS)	Claims	8, 10, 11, 18-22, 24-27	YES
	Claims	1-7, 9, 12-17, 23	NO
Industrial applicability (IA)	Claims	1-27	YES
	Claims		NO

2. Citations and explanations:

Document 1: JP, 2001-200000, A (Air Water Inc.), 24 July, 2001 (24.07.01)
Document 2: JP, 8-009992, A (Hitachi Plant Engineering & Construction Co., Ltd.), 16 January, 1996 (16.01.96)
Document 3: JP, 2002-001068, A (Kurita Water Industries Ltd.), 08 January, 2002 (08.01.02)
Document 4: JP, 9-510200, A (Minnesota Mining and Manufacturing Company), 14 October, 1997 (14.10.97)
Document 5: JP, 58-094858, A (Asahi Medical Co., Ltd.), 06 June, 1983 (06.06.83)
Document 6: JP, 2001-524839 (Josutora Bentorei Inc.), 04 December, 2001 (04.12.01)
Document 7: JP, 63-087984, A (Miles Laboratories, Inc.), 19 April, 1988 (19.04.88)
Document 8: Journal of Chromatography (1989), Vol. 476, pages 377 to 389

(Novelty)

Document 1 (Figs. 2 and 3) describes an apparatus separating and fractionating proteins using a membrane, wherein the apparatus is an apparatus of a closed system comprising a purifying filtration section performing filtration, a concentration section performing concentration, a collection section and a pump.

Thus, the subject matters of claims 1, 2, 4, 6 and 7 of this application do not appear to be novel, since they are described in document 1.

Document 2 (Fig. 1) describes an apparatus collecting proteins using a membrane, wherein the apparatus is an apparatus of a closed system comprising a filtration section, a concentration section, a collection section (filtrate storage tank) and a pump.

Thus, the subject matters of claims 1, 2, 4, 6 and 7 of this application do not appear to be novel, since they are described in document 2.

(Inventive Step)

Document 3 describes a membrane separation method and apparatus, and particularly, paragraph [0008] describes that a protein is contained as a solute, paragraph [0009] describes membranes for separating high-molecular substances of proteins and the like include hollow fiber membranes, and paragraph [0017] describes that modules partitioned into a concentration chamber and a penetrating liquid chamber by a semipermeable membrane are provided in multiple stages to achieve enrichment of a target.

Document 4 describes a method for separating a biopolymer, wherein a filter cartridge is employed as a membrane for use in filtration, and wherein the system is a closed system (claim 1, etc,).

Document 5 describes an apparatus treating a plasma protein by filtration, wherein a roller pump is used in the system of the apparatus (see drawings).

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Since documents 1-5 belong to a common technical field in the sense that proteins are separated and fractionated using a filtration membrane, a person skilled in the art could easily conceive that a hollow fiber membrane is employed as a membrane, the filtration membrane is adapted to have multiple stages, a roller type pump is employed as a liquid feeding pump, and a cartridge is employed as a filtration section, and the amount of liquid in a circuit is merely a matter of design variation that is determined by a person skilled in the art in consideration of the amount of treated liquid and the scale of equipment. Even though these components are integrated into an apparatus as one system, they merely perform functions which they originally have, and a predictable effect is not found to be exhibited. Accordingly, the subject matters of claims 1-7, 9 and 12-14 of this application do not appear to involve an inventive step, since they could have been easily achieved from the inventions described in documents 1-4.

Document 6 describes an apparatus performing removal of a specific object and filtration at the same time, wherein the apparatus uses an adsorbent with an antibody coupled to a base sized so as not to pass through a membrane, and further comprises a hollow filter plasma separating membrane capable of removing water, a liquid and a low-molecular solute.

Since the molecular weight of human α1 micro-globulin had been well known before the date of priority of this application, a person skilled in the art would generally adjust the permeability and the diameter of the membrane in consideration of the molecular weights of a plurality of proteins existing in a mixed solution and the molecular weights of proteins to be fractionated, and setting these values to be within the range of numerical values described in claim 15 of this application is not found to be noticeably technically difficult.

Thus, the subject matters of claims 15-17 and 23 of this application do not appear to involve an inventive step, since they could have been easily achieved by a person skilled in the art from the inventions described in documents 6 and 7.

(Novelty, Inventive Step and Industrial Applicability)

Since cited documents 1-5 neither describes nor suggest providing a "buffering section" in a system in an apparatus for separating a protein, the subject matters of claims 8, 10 and 11 of this application appear to be novel, to involve an inventive step and to be industrially applicable.

Document 6 neither describes nor suggests that an antibody is fixed on the membrane surface of a membrane separation system.

Thus, the subject matters of claims 18-22 of this application appear to be novel, to involve an inventive step and to be industrially applicable.

Document 8 describes that if acetonitrile is added to an elution buffer for carrying out powerful cationic ion exchange chromatography, a nonspecific hydrophobic interaction between a peptide and a column is inhibited, and resultantly, the electric charge of the peptide is proportional to the holding time.

However, the document does not describe that an organic solvent is added in a solution when fractionating a target protein by a protein separating membrane, and a person skilled in the art could not predict that the nonspecific interaction between the membrane and the protein is resultantly inhibited to improve a collection rate.

Thus, the subject matters of claims 24-27 of this application appear to be novel, involve an inventive step and to be industrially applicable.